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Frank C. Eisenschenk, Ph.D., Patent Attorney

REQUEST FOR CERTIFICATE OF
CORRECTION UNDER 37 CFR 1.322
Docket No. ISI.103

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Simon Davis
Issued : December 14, 2010
Patent No. : 7,851,598
Conf. No. : 4177
For : Receptor Modulators

Mail Stop Certificate of Corrections Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 CFR 1.322 (OFFICE MISTAKE)

Sir:

A Certificate of Correction for the above-identified patent has been prepared and is attached hereto.

In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:

Column 8, line 33:

“(Yxx/Ix₇₋₁₂YxxL/I)”

Column 13, line 13:

“(http://www.ncbi.nhn.nih.gov/)”

Application Reads:

Page 12, line 15:

--(YxxL/Ix₇₋₁₂YxxL/I)--

Page 20, line 2:

--(http://www.ncbi.nlm.nih.gov)--

Column 18, line 11:

“cysteine ● HC1”

Page 27, line 25:

--cysteine●HC1--

Column 18, line 14:

“cysteine-HC1”

Page 27, line 28:

--cysteine●HC1--

Column 22, Table 1, Column “Protein”:

“hpd-1”

Page 34, Table 1, Column “Protein”:

--hPD-1--

Column 45, Table 4, Row “ATOM 890”:

“41.625”

Page 52, Table 4, Row “ATOM 890”:

--41.525--

Column 49, Table 4, Row “ATOM 1016”:

“46.58”

Page 55, Table 4, Row “ATOM 1016”:

--46.88--

Column 133, Table 5, line 11:

“tattatttc tgggtcgagga”

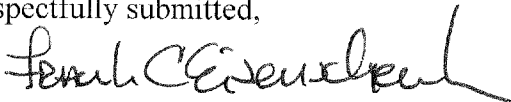
Page 116, Table 5, line 11:

--tattatttc tgggtgagga--.

A true and correct copy of pages 12, 20, 27, 34, 52, 55, and 116 of the specification as filed which support Applicant's assertion of the errors on the part of the Patent Office accompanies this Certificate of Correction.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,



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Attachments: Copy of pages 12, 20, 27, 34, 52, 55, and 116 of the specification
Certificate of Correction

only the C'-D loop of CD28. The second type of chimeric protein may be one which does not bind to any portion of the C'-D loop of CD28. The second type of chimeric protein may or may not bind to the C'-D loop (or the equivalent loop) of any other member of the CD28 family of proteins. The second type of protein may or may not
5 bind to any or all of the sequences shown in Table 3.

Receptors bound by the antibody and chimeric protein

The receptors which are bound by the antibody or chimeric protein of the invention are expressed on the cell surface. The receptor is capable of being
10 phosphorylated (typically at one or more tyrosine residues in the cytoplasmic region of the receptor), and phosphorylation of the receptor will typically lead to its activation. The receptor will comprise a cytoplasmic domain that is dependent on extrinsic protein kinases to be phosphorylated. Thus the receptor will not have an intrinsic enzymatic (kinase or phosphatase) activity. The receptor will typically
15 comprise tyrosine-containing, activating ITAM motifs (YxxL/Ix₇₋₁₂YxxL/I), inhibitory ITIM motifs (I/V/L/SxYxxL/V) or "switch" (TxYxxV/I; activating and inhibitory) signalling motifs (where x is any amino acid). These motifs are phosphorylated by cytoplasmic tyrosine kinases, such as the Src kinases, in competition with antagonistic tyrosine phosphatases, such as CD45. The signalling
20 character of the receptors is defined exclusively by the nature of these motifs (ITAM vs ITIM: activating vs inhibitory).

The receptor may be a member of any surface protein superfamily, but is typically a member of the immunoglobulin superfamily. The receptor may be a member of the CD28 superfamily. The receptor may be any of the specific receptors
25 which are shown in Table 1 or 2 or may comprise a sequence which is homologous to the sequence of any of these specific receptors. The receptor may be CD28, CTLA-4, ICOS, PD-1 or BTLA or comprise a sequence which is homologous to the sequence of any of these specific receptors.

The receptor may be of any of the species that are mentioned herein, and thus
30 may be a mammalian or avian, preferably rodent (such as mouse or rat) or primate (such as human) receptor.

Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pair (HSPs) by identifying short words of length W in the query sequence that either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighbourhood word score threshold (Altschul *et al*, supra). These initial neighbourhood word hits act as seeds for initiating searches to find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extensions for the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1992) *Proc. Natl. Acad. Sci. USA* 89: 10915-10919) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

The BLAST algorithm performs a statistical analysis of the similarity between two sequences; see e.g., Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90: 5873-5787. One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two amino acid sequences would occur by chance. For example, a sequence is considered similar to another sequence if the smallest sum probability in comparison of the first sequence to the second sequence is less than about 1, preferably less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

The homologous sequence typically differs by at least 1, 2, 5, 10, 20 or more mutations (each of which may be a substitution, deletion or insertion of an amino acid). These mutations may be measured across any of the regions mentioned above in relation to calculating homology. The substitutions are preferably conservative substitutions. These are defined according to the following Table. Amino acids in

(v) *Purification of the CD28 homodimer*

The pH of the thrombin-cleaved protein was adjusted to pH 8.5 using 2.75M Tris pH 8.5, prior to concentration to 0.5 ml using a Centriprep 10 concentrator (Millipore Corp). Fresh Protein A beads were washed and rehydrated to a final volume of ~5 mls, prior to being packed into a 0.7 cm x 20 cm Econo-column (Bio-Rad, U.K.) and then equilibrated with HBS, pH 8.5 at 4°C. The concentrated protein was then applied to the column, allowed to run into the bed, and then sequential fractions were eluted by addition of 0.5 ml of HBS, pH 8.5 to the top of the bed every 10 minutes for 2h. The absorbance of each fraction was determined at 280 nm. The extent of separation of the Fc from the thrombin-released CD28 homodimer was determined by 12% SDS-PAGE analysis of the fractions under non-reducing conditions. The critical steps for good separation were (1) to allow the protein to pass slowly through the column and (2) to conduct the separation at 4°C. The homodimer was concentrated to 0.5 ml and subjected to gel-filtration on a Superdex 75 H/R column (Amersham Biosciences). The purified homodimer was used for crystallization trials, reduced and alkylated for other crystallization trials (see below), or frozen at -80°C for future use.

Preparation of Fab fragments of 5.11A1 antibody

Fab fragments were prepared using the Pierce Biotechnology ImmunoPure® Fab Preparation Kit, as briefly outlined below.

(i) *Fab fragment generation and purification*

Nine millilitres of whole, purified 5.11A1 antibody at 0.3 mg/ml in PBS was concentrated to 1 ml and then diluted to 10 mls with 20 mM sodium phosphate, 10 mM EDTA, pH 7 and then re-concentrated to 0.5 ml. To this was added 0.5 ml of 20 mM sodium phosphate, pH 7 containing 3.5 mg/ml cysteine•HCl. The 1 ml mixture was then added to 0.5 ml of a 50% slurry of Sepharose-immobilized Papain supplied with the kit, which had been pre-equilibrated with 20 mM sodium phosphate pH 7 containing 3.5 mg/ml cysteine•HCl. This was then incubated for 5 hours in a shaking water bath at 37°C. The cleaved Fab and Fc fragments and undigested IgG were separated from the Immobilized Papain beads by centrifugation at 1000g and the beads rinsed with 1.5 ml of the ImmunoPure IgG Binding Buffer supplied with the kit. The wash was then combined with the crude digest and the mix applied to a Sepharose-immobilized Protein

Table 1
CD28 family superagonistic epitopes
Epitopes are named according to the strands from which they derive.

| Protein | A' | B | C-C' | C''-D | E | F | G |
|---------|-------|--------|-----------------|--------------|-------|--------|---------|
| hCD28 | SPMLV | AVNLS | SLHKGLDSAVEVCV | VYSKTGFNCDDG | FYLQN | TDIYFC | NGTIHV |
| hCTLA-4 | PAVVL | GIASFV | TVLRQADSQVTEVCA | FLDDSICTG | LTIQG | TGLYIC | NGTQIVV |
| hICOS | YEMFI | GVQIL | QLLKGGQILCD | VSIKSLKFCHS | FFLYN | ANYYFC | TGGYIHI |

PD-1 and BTLA superagonistic epitopes

| Protein | A | B | C-C' | C''-D | E | F | G |
|---------|--------|-------|------------|-----------|-------|--------|--------|
| hPD-1 | PALLVV | DNATF | RMSPSNQTDK | QPGQDCRFR | MSVVR | NDSGTY | LRAELR |
| hBTLA | QSEHSI | DPFEL | KLNG | QTSWK | LHFEP | NDNGSY | TTLYVT |

Table 3

| Protein | Sequence |
|---------|-----------------|
| hCD28 | GNYSQQIQVYSKTGF |
| hCTLA-4 | YMMGNELTFLDDS |
| hICOS | KTKGSGNTVSIKSLK |
| hPD-1 | LAAPEDRSQPGQDCR |

| | | | | | | | | | | |
|------|-----|-----|-----|-----|---------|--------|--------|------|-------|---|
| ATOM | 842 | CB | ASP | 110 | 158.395 | 60.740 | 62.082 | 1.00 | 68.55 | L |
| ATOM | 843 | CG | ASP | 110 | 157.861 | 61.528 | 60.889 | 1.00 | 84.17 | L |
| ATOM | 844 | OD1 | ASP | 110 | 156.656 | 61.399 | 60.580 | 1.00 | 78.11 | L |
| ATOM | 845 | OD2 | ASP | 110 | 158.641 | 62.277 | 60.256 | 1.00 | 94.16 | L |
| ATOM | 846 | C | ASP | 110 | 158.022 | 58.731 | 63.551 | 1.00 | 60.38 | L |
| ATOM | 847 | O | ASP | 110 | 158.093 | 58.882 | 64.776 | 1.00 | 54.97 | L |
| ATOM | 848 | N | ALA | 111 | 158.487 | 57.651 | 62.932 | 1.00 | 55.72 | L |
| ATOM | 849 | CA | ALA | 111 | 159.151 | 56.577 | 63.661 | 1.00 | 59.37 | L |
| ATOM | 850 | CB | ALA | 111 | 158.123 | 55.633 | 64.272 | 1.00 | 55.98 | L |
| ATOM | 851 | C | ALA | 111 | 160.074 | 55.815 | 62.730 | 1.00 | 51.95 | L |
| ATOM | 852 | O | ALA | 111 | 159.669 | 55.363 | 61.658 | 1.00 | 59.98 | L |
| ATOM | 853 | N | ALA | 112 | 161.328 | 55.685 | 63.141 | 1.00 | 47.00 | L |
| ATOM | 854 | CA | ALA | 112 | 162.318 | 54.977 | 62.348 | 1.00 | 42.20 | L |
| ATOM | 855 | CB | ALA | 112 | 163.712 | 55.266 | 62.887 | 1.00 | 43.77 | L |
| ATOM | 856 | C | ALA | 112 | 162.043 | 53.476 | 62.376 | 1.00 | 42.23 | L |
| ATOM | 857 | O | ALA | 112 | 161.447 | 52.957 | 63.325 | 1.00 | 45.43 | L |
| ATOM | 858 | N | PRO | 113 | 162.464 | 52.761 | 61.325 | 1.00 | 51.11 | L |
| ATOM | 859 | CD | PRO | 113 | 163.153 | 53.256 | 60.117 | 1.00 | 52.49 | L |
| ATOM | 860 | CA | PRO | 113 | 162.250 | 51.316 | 61.269 | 1.00 | 49.74 | L |
| ATOM | 861 | CB | PRO | 113 | 162.267 | 51.018 | 59.776 | 1.00 | 32.76 | L |
| ATOM | 862 | CG | PRO | 113 | 163.223 | 52.029 | 59.220 | 1.00 | 41.64 | L |
| ATOM | 863 | C | PRO | 113 | 163.356 | 50.568 | 61.997 | 1.00 | 45.33 | L |
| ATOM | 864 | O | PRO | 113 | 164.511 | 50.988 | 61.974 | 1.00 | 53.16 | L |
| ATOM | 865 | N | THR | 114 | 163.006 | 49.475 | 62.661 | 1.00 | 36.71 | L |
| ATOM | 866 | CA | THR | 114 | 164.009 | 48.675 | 63.341 | 1.00 | 39.49 | L |
| ATOM | 867 | CB | THR | 114 | 163.505 | 48.159 | 64.706 | 1.00 | 34.54 | L |
| ATOM | 868 | OG1 | THR | 114 | 162.504 | 47.153 | 64.511 | 1.00 | 38.54 | L |
| ATOM | 869 | CG2 | THR | 114 | 162.926 | 49.305 | 65.518 | 1.00 | 31.63 | L |
| ATOM | 870 | C | THR | 114 | 164.322 | 47.515 | 62.406 | 1.00 | 42.88 | L |
| ATOM | 871 | O | THR | 114 | 163.527 | 46.585 | 62.247 | 1.00 | 35.53 | L |
| ATOM | 872 | N | VAL | 115 | 165.488 | 47.596 | 61.769 | 1.00 | 36.33 | L |
| ATOM | 873 | CA | VAL | 115 | 165.939 | 46.594 | 60.815 | 1.00 | 42.49 | L |
| ATOM | 874 | CB | VAL | 115 | 166.973 | 47.210 | 59.839 | 1.00 | 46.96 | L |
| ATOM | 875 | CG1 | VAL | 115 | 167.217 | 46.269 | 58.670 | 1.00 | 26.72 | L |
| ATOM | 876 | CG2 | VAL | 115 | 166.470 | 48.555 | 59.338 | 1.00 | 30.46 | L |
| ATOM | 877 | C | VAL | 115 | 166.544 | 45.324 | 61.424 | 1.00 | 38.71 | L |
| ATOM | 878 | O | VAL | 115 | 167.064 | 45.327 | 62.541 | 1.00 | 36.49 | L |
| ATOM | 879 | N | SER | 116 | 166.458 | 44.237 | 60.659 | 1.00 | 44.76 | L |
| ATOM | 880 | CA | SER | 116 | 166.988 | 42.939 | 61.053 | 1.00 | 51.12 | L |
| ATOM | 881 | CB | SER | 116 | 165.975 | 42.188 | 61.913 | 1.00 | 55.78 | L |
| ATOM | 882 | OG | SER | 116 | 165.653 | 42.932 | 63.068 | 1.00 | 58.23 | L |
| ATOM | 883 | C | SER | 116 | 167.292 | 42.130 | 59.799 | 1.00 | 44.61 | L |
| ATOM | 884 | O | SER | 116 | 166.413 | 41.891 | 58.976 | 1.00 | 53.07 | L |
| ATOM | 885 | N | ILE | 117 | 168.547 | 41.726 | 59.641 | 1.00 | 40.79 | L |
| ATOM | 886 | CA | ILE | 117 | 168.935 | 40.929 | 58.487 | 1.00 | 35.02 | L |
| ATOM | 887 | CB | ILE | 117 | 170.299 | 41.393 | 57.902 | 1.00 | 20.96 | L |
| ATOM | 888 | CG2 | ILE | 117 | 171.426 | 41.040 | 58.848 | 1.00 | 28.48 | L |
| ATOM | 889 | CG1 | ILE | 117 | 170.529 | 40.742 | 56.537 | 1.00 | 16.89 | L |
| ATOM | 890 | CD1 | ILE | 117 | 171.461 | 41.525 | 55.632 | 1.00 | 18.50 | L |
| ATOM | 891 | C | ILE | 117 | 169.039 | 39.484 | 58.952 | 1.00 | 32.15 | L |
| ATOM | 892 | O | ILE | 117 | 169.467 | 39.212 | 60.076 | 1.00 | 40.81 | L |
| ATOM | 893 | N | PHE | 118 | 168.626 | 38.560 | 58.091 | 1.00 | 28.82 | L |
| ATOM | 894 | CA | PHE | 118 | 168.671 | 37.145 | 58.423 | 1.00 | 22.76 | L |

| | | | | | | | | | | |
|------|------|-----|-----|-----|---------|--------|--------|------|-------|---|
| ATOM | 1001 | O | VAL | 133 | 166.701 | 39.222 | 56.454 | 1.00 | 24.39 | L |
| ATOM | 1002 | N | CYS | 134 | 165.206 | 40.404 | 55.254 | 1.00 | 24.79 | L |
| ATOM | 1003 | CA | CYS | 134 | 165.412 | 41.626 | 55.999 | 1.00 | 33.03 | L |
| ATOM | 1004 | C | CYS | 134 | 164.070 | 42.163 | 56.444 | 1.00 | 34.77 | L |
| ATOM | 1005 | O | CYS | 134 | 163.166 | 42.338 | 55.631 | 1.00 | 37.02 | L |
| ATOM | 1006 | CB | CYS | 134 | 166.104 | 42.660 | 55.127 | 1.00 | 37.32 | L |
| ATOM | 1007 | SG | CYS | 134 | 166.705 | 44.083 | 56.077 | 1.00 | 64.48 | L |
| ATOM | 1008 | N | PHE | 135 | 163.946 | 42.420 | 57.737 | 1.00 | 28.41 | L |
| ATOM | 1009 | CA | PHE | 135 | 162.710 | 42.949 | 58.296 | 1.00 | 35.98 | L |
| ATOM | 1010 | CB | PHE | 135 | 162.297 | 42.152 | 59.536 | 1.00 | 23.45 | L |
| ATOM | 1011 | CG | PHE | 135 | 161.854 | 40.746 | 59.244 | 1.00 | 41.99 | L |
| ATOM | 1012 | CD1 | PHE | 135 | 160.991 | 40.472 | 58.187 | 1.00 | 58.79 | L |
| ATOM | 1013 | CD2 | PHE | 135 | 162.280 | 39.696 | 60.049 | 1.00 | 38.90 | L |
| ATOM | 1014 | CE1 | PHE | 135 | 160.555 | 39.170 | 57.939 | 1.00 | 56.32 | L |
| ATOM | 1015 | CE2 | PHE | 135 | 161.849 | 38.391 | 59.810 | 1.00 | 57.18 | L |
| ATOM | 1016 | CZ | PHE | 135 | 160.987 | 38.127 | 58.753 | 1.00 | 46.88 | L |
| ATOM | 1017 | C | PHE | 135 | 162.880 | 44.412 | 58.696 | 1.00 | 37.21 | L |
| ATOM | 1018 | O | PHE | 135 | 163.841 | 44.773 | 59.373 | 1.00 | 31.75 | L |
| ATOM | 1019 | N | LEU | 136 | 161.951 | 45.253 | 58.264 | 1.00 | 38.27 | L |
| ATOM | 1020 | CA | LEU | 136 | 161.968 | 46.665 | 58.622 | 1.00 | 33.10 | L |
| ATOM | 1021 | CB | LEU | 136 | 162.049 | 47.531 | 57.369 | 1.00 | 23.62 | L |
| ATOM | 1022 | CG | LEU | 136 | 163.303 | 47.259 | 56.534 | 1.00 | 17.58 | L |
| ATOM | 1023 | CD1 | LEU | 136 | 163.055 | 46.103 | 55.572 | 1.00 | 17.79 | L |
| ATOM | 1024 | CD2 | LEU | 136 | 163.686 | 48.512 | 55.770 | 1.00 | 29.81 | L |
| ATOM | 1025 | C | LEU | 136 | 160.632 | 46.839 | 59.319 | 1.00 | 30.65 | L |
| ATOM | 1026 | O | LEU | 136 | 159.600 | 47.002 | 58.673 | 1.00 | 30.43 | L |
| ATOM | 1027 | N | ASN | 137 | 160.651 | 46.779 | 60.643 | 1.00 | 35.92 | L |
| ATOM | 1028 | CA | ASN | 137 | 159.421 | 46.873 | 61.400 | 1.00 | 43.25 | L |
| ATOM | 1029 | CB | ASN | 137 | 159.387 | 45.751 | 62.433 | 1.00 | 42.56 | L |
| ATOM | 1030 | CG | ASN | 137 | 159.308 | 44.384 | 61.793 | 1.00 | 30.61 | L |
| ATOM | 1031 | OD1 | ASN | 137 | 159.471 | 43.356 | 62.454 | 1.00 | 37.72 | L |
| ATOM | 1032 | ND2 | ASN | 137 | 159.057 | 44.363 | 60.490 | 1.00 | 39.03 | L |
| ATOM | 1033 | C | ASN | 137 | 159.101 | 48.199 | 62.075 | 1.00 | 40.01 | L |
| ATOM | 1034 | O | ASN | 137 | 159.975 | 49.028 | 62.305 | 1.00 | 39.51 | L |
| ATOM | 1035 | N | ASN | 138 | 157.813 | 48.362 | 62.370 | 1.00 | 41.07 | L |
| ATOM | 1036 | CA | ASN | 138 | 157.239 | 49.526 | 63.036 | 1.00 | 38.43 | L |
| ATOM | 1037 | CB | ASN | 138 | 157.227 | 49.273 | 64.540 | 1.00 | 34.91 | L |
| ATOM | 1038 | CG | ASN | 138 | 156.667 | 47.916 | 64.883 | 1.00 | 33.75 | L |
| ATOM | 1039 | OD1 | ASN | 138 | 155.592 | 47.806 | 65.459 | 1.00 | 29.26 | L |
| ATOM | 1040 | ND2 | ASN | 138 | 157.402 | 46.864 | 64.537 | 1.00 | 33.12 | L |
| ATOM | 1041 | C | ASN | 138 | 157.838 | 50.898 | 62.749 | 1.00 | 31.73 | L |
| ATOM | 1042 | O | ASN | 138 | 158.582 | 51.447 | 63.559 | 1.00 | 39.37 | L |
| ATOM | 1043 | N | PHE | 139 | 157.492 | 51.458 | 61.599 | 1.00 | 32.60 | L |
| ATOM | 1044 | CA | PHE | 139 | 157.982 | 52.770 | 61.227 | 1.00 | 34.36 | L |
| ATOM | 1045 | CB | PHE | 139 | 159.138 | 52.644 | 60.237 | 1.00 | 37.95 | L |
| ATOM | 1046 | CG | PHE | 139 | 158.770 | 51.972 | 58.946 | 1.00 | 21.99 | L |
| ATOM | 1047 | CD1 | PHE | 139 | 158.295 | 52.716 | 57.869 | 1.00 | 28.23 | L |
| ATOM | 1048 | CD2 | PHE | 139 | 158.941 | 50.597 | 58.792 | 1.00 | 23.34 | L |
| ATOM | 1049 | CE1 | PHE | 139 | 157.998 | 52.102 | 56.651 | 1.00 | 22.39 | L |
| ATOM | 1050 | CE2 | PHE | 139 | 158.646 | 49.969 | 57.578 | 1.00 | 15.56 | L |
| ATOM | 1051 | CZ | PHE | 139 | 158.175 | 50.723 | 56.505 | 1.00 | 21.70 | L |
| ATOM | 1052 | C | PHE | 139 | 156.868 | 53.626 | 60.627 | 1.00 | 42.27 | L |
| ATOM | 1053 | O | PHE | 139 | 155.772 | 53.142 | 60.350 | 1.00 | 50.50 | L |

Table 5

DNA sequence of human CD28 cDNA

| | | | | | | |
|-------------|------------|------------|-------------|------------|-------------|------|
| agactctcag | gccttggcag | gtgcgtcttt | cagttccctt | cacacttcgg | gttcctcggg | 60 |
| gaggaggggc | tggaacccta | gcccacgctc | aggacaaaga | tgtcaggct | gctcttggct | 120 |
| ctcaacttat | tcccttcaat | tcaagtaaca | ggaacaaga | ttttggtgaa | gcagtcgccc | 180 |
| atgctttag | cgtacgacaa | tgcggtcaac | cttagctgoa | agtattccta | caatctcttc | 240 |
| tcaagggagt | tccgggcac | ccttcacaaa | ggactggata | gtgctgtgga | agtctgtgtt | 300 |
| gtatatggga | attactccca | gcagcttcag | gtttactcaa | aaacggggtt | caactgtgat | 360 |
| gggaaattgg | gcaatgaatc | agtgacattc | tacctccaga | atttgtatgt | taaccaaaaca | 420 |
| gatattttact | tctgcaaaat | tgaagttatg | tatctctctc | cttacctaga | caatgagaag | 480 |
| agcaatggaa | ccattatcca | tgtgaaaggg | aaacaccttt | gtccaagtcc | cctatttccc | 540 |
| ggaccttcta | agcccttttg | ggtgctgggt | gtggttgggt | gagtcctggc | ttgctatagc | 600 |
| ttgctagtaa | cagtggcctt | tattattttc | tgggtgagga | gtaagaggag | caggctcctg | 660 |
| cacagtgaact | acatgaacat | gactccccgc | cgccccgggc | ccaccgcaa | gcattaccag | 720 |
| cctatgccc | caccacgga | cttcgcagcc | tatcgtctct | gacacggacg | cctatccaga | 780 |
| agccagccgg | ctggcagccc | ccatctgctc | aatatcactg | ctctggatag | gaaatgaccg | 840 |
| ccatctccag | ccggccacct | cagccctgt | tgggcccacca | atgccaat | ttctcgagt | 900 |
| actagaccaa | atatcaagat | cattttgaga | ctctgaaatg | aagtaaaaga | gatttctgt | 960 |
| gacaggccaa | gtcttacagt | gccatggccc | acattccaac | ttaccatgta | cttagtgact | 1020 |
| tgactgagaa | gttagggtag | aaaacaaaaa | gggagtggat | tctgggagcc | tcttcccttt | 1080 |
| ctcactcacc | tgcacatctc | agtcaagcaa | agtgtgggat | ccacagacat | tttagttgca | 1140 |
| gaagaaaggc | taggaaatca | ttccttttgg | ttaaatgggt | gtttaatctt | ttggttagtg | 1200 |
| ggttaaacgg | ggtaagttag | agtaggggga | gggataggaa | gacatattta | aaaaccatta | 1260 |
| aaacactgtc | tccactcat | gaaatgagcc | acgtagtctc | tatttaatgc | tgttttcctt | 1320 |
| tagtttagaa | atacatagac | attgtctttt | atgaattctg | atcatattta | gtcattttga | 1380 |
| ccaaatgagg | gatttggtca | aatgagggat | tccctcaaag | caatatcagg | taaaccaagt | 1440 |
| tgctttcctc | actccctgtc | atgagacttc | agtgttaatg | ttcacaatat | actttcgaaa | 1500 |
| gaataaaata | gttc | | | | | 1514 |

Amino acid sequence of human CD28 (SEQ ID NO:1)

MLRLLALNL FPSIQVTGNK ILVKQSPMLV AYDNAVNLSK KYSYNLFSRE FRASLHKGLD
 SAVEVCVVYQ NYSQQQLQVYS KTGFNCDGKL GNESVTFFYLQ NLYVNQTDIY FCKIEVMYPP
 PYLDNEKSNG **TIHVKGKHL** CPSPLFPGPS KPFWVLVVVG GVLACYSLLV TVAFIIFWVR
 SKRSRLHSD YMNMTPRRPG PTRKHYQPYA PPRDFAAYRS

The extracellular domain is shown in bold

The stalk region is underlined

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,851,598

Page 1 of 2

APPLICATION NO.: 10/585,491

DATED : December 14, 2010

INVENTOR : Simon Davis

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 8,

Line 33, “(Yxx/Ix₇₋₁₂YxxL/I)” should read --(YxxL/Ix₇₋₁₂YxxL/I)--.

Column 13,

Line 13, “(http://www.ncbi.nhn.nih.gov/)” should read
--(http://www.ncbi.nlm.nih.gov)--.

Column 18,

Line 11, “cysteine ● HC1” should read -- cysteine●HC1--.

Line 14, “cysteine-HC1” should read --cysteine●HC1--.

Column 22,

Table 1, Column “Protein”, “hpd-1” should read --hPD-1--.

Column 45,

Table 4, Row “ATOM 890”, “41.625” should read --41.525--.

Column 49,

Table 4, Row “ATOM 1016”, “46.58” should read --46.88--.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,851,598

Page 2 of 2

APPLICATION NO.: 10/585,491

DATED : December 14, 2010

INVENTOR : Simon Davis

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 133,

Table 5, Line 11, "tattatttc tgggtcgagga" should read --tattatttc tgggtgagga--.

MAILING ADDRESS OF SENDER:

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